

AF

PATENT SPECIFICATION

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COMPLETE SPECIFICATION

Synthetic Lactide Copolymer Ribbons and Filaments

We, E. I. DU PONT DE NEMOURS AND COMPANY, a Corporation organized and existing under the laws of the State of Delaware, United States of America, of Wilmington 98, Delaware, United States of America, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to synthetic lactide copolymer filaments and ribbons and provides articles of this class, made from certain lactide copolymers, which are specially suitable for use in surgical applications as or in sutures and other structures used in joining or supporting living tissues.

In this specification, unless otherwise stated, all parts proportions and percentages are by weight.

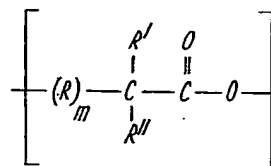
Catgut (actually from sheep intestine) is the most commonly used absorbable suture now on the market. In many instances, however, it causes adverse tissue reaction in the sutured flesh. This, together with the fact that it is expensive, nonuniform both in cross section and composition, and requires storage under moist conditions, makes it far from an ideal suture material. Nylon, stainless steel, cotton, linen, ramie, "Teflon" (registered trade-mark) fluorocarbon resin, "Dacron" (registered trade-mark) polyester fibres, silk, and other materials have been suggested and/or used as surgical sutures. Some of them have advantages over catgut in strength, uniformity and storage characteristics, but they are not absorbed by living tissue.

Among the requirements of the ideal absorbable suture product are that it should handle properly, should not create a situation favourable to bacterial growth, should have adequate tensile strength, should not tear flesh, should be controllably uniform in properties, including dimensional stability within the body, should be sterilizable, should be absorbable

by living tissue, preferably at a constant rate regardless of the place in the body and the condition of the patient, without causing such unfavourable tissue reactions as walling off, granulation or excessive oedema, and finally should be capable of tying and holding surgical knots properly.

This invention fulfils the above requirements to a remarkable degree by providing highly oriented, high tenacity filaments of certain copolymers of lactides, the filaments having excellent dimensional stability in body tissue and preferably retracting less than 15% in an accelerative test in which the filaments are immersed in water at 77°C. for a period of five minutes.

The oriented filaments or ribbons of the invention are composed of a lactide copolymer containing 85 to 98.5% of repeating units of a single antipodal species of alpha hydroxy propionic acid and 1.5 to 15% of repeating units of the formula:



where R is lower alkylene, m is 0 or 1, R' is a hydrogen atom or a lower alkyl group, and R'', which can be the same as or different from R', is a hydrogen atom or an alkyl group of up to 22 carbons when m is zero and, when m is 1, R'' is a hydrogen atom or a lower alkyl group, lower, herein meaning having up to 6 carbon atoms, and the repeating units of the said formula including at least one which is different from that derived from the said antipodal species, said copolymer before being oriented having an inherent viscosity of at least 1.0 at 0.1% concentration in benzene at 25°C. and said filament losing

at least 20% of its weight on treatment with boiling water for a period of 100 hours.

- 5 Preferably the copolymers have an inherent viscosity of at least 1.2, as determined at 0.1% concentration in benzene at 25°C. prior to being oriented. Preferably, because of availability of starting materials, the repeating units of the formula specified above are derived from α -hydroxycarboxylic acids, i.e., units of the above formula in which m is zero. Most preferred, because of the properties of the sutures made therefrom, are repeating or comonomer units derived from glycolide or DL-lactide, i.e., repeating units of formula (1) in which m is 0, R' is hydrogen or methyl, and R'' is hydrogen. In other words, the number of carbon atoms in the repeating unit is 2 to 24, preferably 2 to 8, and most preferably 2 to 3. It will be understood that when m is zero, R' is methyl, and R'' is hydrogen, the repeating unit in the above formula may be derived from DL-lactide.

- 10 Illustrative of the comonomers which can be employed with the lactide providing the single antipodal species referred to above, to form copolymers useful in preparing the filaments of this invention, there can be named glycolide, β -propiolactone, tetramethylglycolide, β -butyrolactone, γ -butyrolactone, pivalolactone, and intermolecular cyclic esters of α -hydroxybutyric acid, α -hydroxyisobutyric acid, α -hydroxyvaleric acid, α -hydroxyisovaleric acid; α -hydroxycaproic acid, α -hydroxy- α -ethylbutyric acid, α -hydroxyisocaproic acid, α -hydroxy- β -methylvaleric acid, α -hydroxyheptanoic acid, α -hydroxyoctanoic acid, α -hydroxydecanoic acid, α -hydroxymyristic acid, α -hydroxystearic acid, and α -hydroxy lignoceric acid.

- 40 The filaments prepared from the above-described lactide copolymers are conveniently formed by melt-extruding the copolymer through a spinneret and then drawing the filaments in one or more stages to at least four times their original length to effect orientation and to improve their tensile strength. The resultant oriented filaments are strong and

retain much of their strength on being tied into surgeon's knots.

To further improve their dimensional stability and particularly tensile strength retention, one may subject them to an annealing treatment. This optional annealing treatment is effected by heating the filament, while holding it essentially taut, at 60°C. to 150°C., and then allowing it to cool to room temperature (25°C.) while held taut. The annealing is preferably conducted for such a time that the filament shows less than 30%, most preferably less than 15%, shrinkage on subsequent immersion, for five minutes without tension, in water at 77°C. The heating step of annealing usually requires from 0.5 to 5 minutes.

A filament which meets the foregoing shrinkage test (77°C.) undergoes substantially no shrinkage when used as a suture in contact with body tissues (see Example II). The conditions of this test are designed to give a quick in vitro measure of the dimensional stability of the filaments that can be projected to their usefulness as suture materials. In this connection, it should be mentioned that the conditions of draw have an influence over the shrinkage. Further, it has been found that even those filaments showing a large amount of shrinkage at 77°C. have relatively little shrinkage at 37°C. (98.6°F), i.e., at body temperature, even after being in contact with distilled water for 10 and 21-day periods.

Since the function of a suture is to hold severed tissue until healing is well along, and to prevent separation as a result of movement or exercise, the suture should have adequate strength. It is particularly important that strength be maintained when knots are tied and during the actual procedure of drawing tight a suitable knot. Catgut is well known to have marginal strength in this respect. In contrast, filaments from the copolymers of the invention, high in molecular weight and in oriented form, are exceptionally strong and most significantly retain a high proportion of their strength at the knot point, as shown in the following table:

TABLE I

| | Tensile Strength (Straight Pull) | % Elongation at Break | Tensile Strength (Surgeon's Knot) (4) | % Loss in Strength, Knot vs. Straight |
|---|--|-----------------------------|--|--|
| Catgut | 50,000 psi (1) | 20 | 29,000 psi | 42 |
| | 44,000 psi (2) | 20 | 27,000 psi | 39 |
| L(-)-lactide γ-butyrolactone (95/5) copolymer | 59,000 psi (3) | 17 | 42,000 psi | 29 |

(1) Chrome gut, 3—0 size (0.008—0.010 inch diameter)

(2) Chrome gut, 2—0 size (0.010—0.013 inch diameter)

(3) After U.S. Pharmacopeia.

(4) Inherent visc. (bulk polymer) = 3.0 (spun filament = 1.6), 10X draw, 0.009 inch diameter.

- As will be apparent from Table I, the inherent viscosity of the spun filament, i.e., the oriented filament, may be somewhat less than that of the bulk polymer or copolymer, for during the drawing operation some degradation of the polymer may occur depending on the drawing conditions employed. If the sutures are sterilized by high energy radiation, there may be a further lowering of the molecular weight of the polymer. However, by starting with copolymers having inherent viscosities of at least 1, the sutures prepared therefrom are entirely satisfactory even though there may be some loss in inherent viscosity due to extrusion and orientation, and possibly sterilization.
- The filaments of this invention are further characterized by their hydrolysis behavior and absorbability. On treatment with boiling water for 100 hours, they lose at least 20, and preferably at least about 50%, of their weight. On treatment with boiling water for a period of 50 hours, the copolymers lose at least about 8% of their weight, and preferably they lose at least about 35% of their weight.
- By varying the type and proportion of comonomer employed, the rate of hydrolysis (absorption) of the suture can be controlled. In contrast to the highly variable absorption rates of catgut, the absorption of the copolymers is relatively more independent of the place in the body where used and of the condition of the patent. Since the hydrolysis rate of a particular lactide copolymer is constant at a fixed temperature, say, at 37°C., absorption can be speeded up, for instance, by using different copolymers. For example, poly-L-lactide was 15.3% absorbed in the back muscle of a rat after 270 days. Under comparable conditions, (-)-lactide/DL-lactide (97/3) copolymer was 18.5% absorbed, L(-)-lactide/DL-lactide (95/5) copolymer was 29.0% absorbed, L(-)-lactide/glycolide (95/5) copolymer was 27.3% absorbed, and chromed catgut was 67% absorbed.
- As already indicated, high tensile strength is an exceedingly desirable characteristic for suture materials. The filaments of the present invention are characterized by having a tensile strength of at least 25,000 psi, preferably above 40,000 psi. Some have tensile strengths ranging up to 100,000 psi and higher. Their knot strengths, expressed in pounds of pull, exceed the minimum limits set for absorbable sutures by the U.S. Pharmacopeia, i.e., from 0.125 lb. for a 1—2 mil filament to 25 lbs. for a 36—40 mil filament.
- In preparing the copolymers from which the filaments of this invention are made, the appropriate intermolecular cyclic ester or intramolecular cyclic ester (lactone) of the hydroxy acid is employed. Subject to the requirement as to the constitution of the copolymer, specified above, these can be derived from pure D(-) or L(+)-lactic acids, the optically inactive DL-lactic acid mixture, mixtures of pure D(-) and (+)-lactic acids, and other alpha, beta, or gamma-hydroxy acids, about which more will be said later. The L(+) form of lactic acid is more readily available than the D(-)-acid and hence is particularly preferred. It is to be understood that the various lactides can be made from the corresponding lactic acids by a variety of published methods including that described in Schneider U.S. 2,703,316.
- In general, the tensile modulus, melting point, and specific rotation of lactic acid copolymers decrease with increasing amounts of the antipode in the mixture. In some cases this is desirable because it leads to filaments which

have improved flexibility, without appreciable sacrifice in strength.

In preparing copolymers, the repeating units derived from comonomers discussed above are introduced by use of the appropriate cyclic esters. For repeating units derived from alpha-hydroxy acids, these are usually the intermolecular cyclic esters containing six-membered rings, e.g., glycolide. For repeating units derived from beta- or gamma-hydroxy acids, the monomeric lactones, e.g., beta-propiolactone and gamma-butyrolactone, are usually used.

In preparing the filaments of this invention, it is essential to use copolymers made from highly purified lactides. For example, for excellent results L(-)-lactide should have a melting point of at least 96°C. and a specific rotation greater than -295°. The polymerization is effected by heating the lactide above its melting point, but below about 215°C. in the presence of a polyvalent metal oxide or compound thereof, under anhydrous conditions in an inert atmosphere.

Specially useful catalysts are zinc oxide, zinc carbonate, basic zinc carbonate, diethylzinc, titanium, magnesium or barium compounds, and litharge.

The proportion and type of catalyst used determine the particular temperature and time required to produce polymer useful for conversion to the filaments of this invention. Thus, the proportion can be as low as 0.01 weight percent or as high as 2 weight percent. As a rule, the lower the proportion of catalyst, the longer the time required to produce polymer of a given inherent viscosity and, conversely, the higher the catalyst concentration, the shorter the time. The best balance is usually obtained employing from 0.02 weight percent to 1 weight percent of catalyst.

In general, it is desirable to agitate the reaction mixture continuously during the polymerization in order to produce a homogeneous polymer at good conversions and to conduct the reaction in two steps, the first being carried out at a lower temperature than the second, or finishing step. Other methods, such as those disclosed in U.S. Patents 2,703,316 and 2,758,987, can be used in making the polymers.

The following is a brief description of a method for preparing the copolymer for conversion to the filaments of this invention: Lactide, purified by several crystallizations from carbon tetrachloride, is placed with one or more solid comonomers in substantially the proportions theoretically required to give a copolymer of the desired formula, in a thoroughly dried reactor equipped with a stirring bar, nitrogen inlet tube, and a drying tube filled conveniently with anhydrous magnesium sulphate or calcium chloride. Nitrogen, which has been dried by passage through anhydrous magnesium sulphate or calcium chloride, is

introduced immediately above the reaction mixture and heating and stirring are started. When the temperature of the reaction mixture has reached about 100°C., the nitrogen inlet is replaced by a thermometer, and from about 0.01 to 2 weight percent of an oxide or salt, of a Group II metal of atomic number 12 to 56, or litharge is added. In the case of copolymerization with a liquid comonomer the liquid comonomer is preferably added after the lactide has melted. Heating is continued until polymer having an inherent viscosity of at least 1 at 0.1% concentration in benzene at 25°C. is obtained. This may require from a few minutes up to 25 or more hours, depending upon the catalyst used.

Polymer, produced as above, may be suitably further treated by cutting it into small pieces, dissolved in a suitable solvent, for example, benzene, toluene, or xylene, and the polymer precipitated by pouring the solution into a large volume of a nonsolvent for the polymer, desirably hexane. The precipitated polymer is removed by filtration, transferred to a blender and a nonsolvent for the polymer is added. The blender is started and after a homogeneous dispersion has been obtained, the dispersion is filtered. The polymer is allowed to dry on the filter, and is then transferred to a vacuum oven. After drying overnight at 100°C., the polymer is removed from the oven and allowed to cool to ambient temperature.

As already indicated, the copolymer material can be converted to filaments by melt-extrusion and also from solution. The diameter of the resulting filaments may be as small as 0.1 mil or less for the individual strands making up the multifilament structures and as large as 45 mils for very heavy monofilament sutures. Generally, however, the filaments of this invention will not have a diameter greater than 20-25 mils. Preferred are monofilaments having diameters of about 1-20 mils and multifilament structures having individual filaments of from less than 0.5 to 2 mils diameter.

It will be understood that spinning and drawing may be done singly or in multiples. To prepare multifilament braided sutures, one may take either monofilaments or groups of filaments to braid.

Spinnerets having orifice sizes of 5 mils or higher, say, up to 150 mils, are suitable for spinning monofils. In spinning from solution, the solution may be extruded either into an atmosphere heated to above the boiling point of the solvent or into a nonsolvent for the polymer, e.g., hexane.

After spinning, the polylactide homo- and copolymer filaments are drawn to effect orientation and to improve tensile strength. This is accomplished by drawing (permanently elongating) the filaments at a temperature between 70°C. and 140°C., preferably between

90°C. and 135°C. the preferred draw ratio being from 5:1 to 11:1. The drawing step may be conducted in one or more steps, in air or in a bath containing a liquid nonsolvent for the polymer, e.g., glycerol or water. This drawing brings about a marked increase in tensile strength and molecular orientation, as measured by the X-ray orientation angle.

Following the drawing, the filaments may be subjected to annealing. This is conveniently carried out by running the oriented filaments from a feed roll to a take-up roll and heating the filaments between the rolls, with the take-up roll rotating at a speed ranging from the same speed of the feed roll to, a speed 4% slower than that of the feed roll. At the first mentioned speed ratio, essentially no shrinkage will take place, and at the second mentioned speed ratio shrinkage will take place up to 4% of its length. As a consequence of this annealing, the filaments undergo essentially no shrinkage under the action of body fluids, when used as sutures.

Instead of spinning the copolymer into filaments, it is possible to extrude or cast it into films, which are then drawn and annealed. The films thus treated can be cut into ribbons, i.e. narrow strips for use as sutures. In the preferred embodiment, however, the sutures are made from filaments.

It is to be understood that minor amounts of inert additives such as coloring materials and plasticizers can be incorporated in the sutures by being mixed with the preformed copolymers by known techniques. Any of a

variety of plasticizers such as, for instance, glyceryl triacetate, ethyl benzoate and diethyl phthalate can be used to advantage, especially with poly-L-lactide. The proportion of plasticizer may vary from 1—40% based on the weight of the polymer. Not only does the plasticizer render the filaments more pliable and more easy to handle, but it also helps in spinning. By the term "inert" is meant materials that are inert chemically to the copolymer, and are inert to living tissue, i.e., do not cause any of the adverse effects discussed on page 2. of this specification.

The invention apart from the essential final step of sterilisation is illustrated by the following Examples:

EXAMPLE I.

A mixture of 95 parts of L(-)-lactide and 5 parts of DL-lactide was fused under nitrogen, and there was added 0.125 part of diethylzinc as a 25% solution in heptane. The mixture was heated at 105°C. for 1 hour at atmospheric pressure in an atmosphere of nitrogen. The solid (L-)-lactide/DL-lactide (95/5) copolymer thus obtained had an inherent viscosity of 2.63 (0.1% solution in benzene at 34.5°C.). The copolymer was ground to a fine powder, which was in turn pressed to a plug suitable for use in an extrusion-spinning apparatus. Filaments of the copolymer were spun at about 200°C. through a 35-mil spinneret and were drawn to 6.4 times their original length in glycerol at about 120°C. The drawn filaments had the following properties:

| | |
|---|------------------------|
| Inherent viscosity: | 1.7 |
| Diameter: | 12.5 mils |
| Tensile Strength: | 58,500 psi |
| Elongation at break: | 20% |
| Modulus: | 1.08×10^6 psi |
| Knot strength: | 37,000 psi |
| Shrinkage after 5 min. in water at 77°C.: | 23% |
| Weight loss after 50 hrs. in boiling water: | 39% |

They were not annealed.

After 30 Days in Distilled Water at 37° C.:

| | |
|---------------------|------------|
| Inherent viscosity: | 0.55 |
| Tensile strength: | 19,000 psi |
| Weight loss: | 2.6% |

After 90 Days in Distilled Water at 37° C.:

| | |
|---------------------|----------|
| Inherent viscosity: | 0.38 |
| Tensile strength: | 5000 psi |
| Weight loss: | 7.0% |

EXAMPLES II—IX.

5 A number of other L(-)- lactide copolymers were prepared and spun into filaments by the method of Example I. When the comonomer was a liquid at ordinary temperature (β -propiolactone, γ -butyrolactone or pivalolac-

tone), it was added to the lactide only after the lactide had been fused. The bulk-polymer properties, spinning conditions, and filament 10 properties of these copolymers are summarized in the following table. The filaments of Example II were not annealed.

TABLE II

| Examples | II | III | IV | V | VI | VII | VIII | IX |
|--|-------------------|-------------------|-------------------|-------------------|--------------------|---------------------------|----------------------------|-------------------|
| % Comonomer | 7.5% DL-lactide | 10% DL-lactide | 15% DL-lactide | 5% glycolide | 10% glycolide | 5% β -propiolactone | 5% γ -butyrolactone | 5% pivalolactone |
| Inh. visc. (bulk) | 2.87 | 2.50 | 2.39 | 2.53 | 2.52 | 1.31 | 2.99 | 2.68 |
| Spinning temp. | 190°C. | 205°C. | 200°C. | 210°C. | 195°C. | — | 170°C. | 170°C. |
| Draw ratio | 8.6 | 8.1 | 7.5 | 8.8 | 8.0 | — | 10 | 10 |
| Drawing temp. | 128°C. | 125°C. | 100°C. | 125°C. | 100°C. | — | 115°C. | 100°C. |
| Inh. visc. (drawn fil.) | 1.75 | 1.75 | 1.47 | 1.84 | 1.70 | — | 1.73 | 1.64 |
| Diameter (mils) | 11.5 | 11.0 | 12.5 | 10.3 | 8.5 | — | 9.4 | 8.5 |
| Ten. strength (psi) | 53,300 | 69,000 | 53,000 | 77,000 | 27,500 | — | 59,000 | 78,000 |
| Elong. at break | 20% | 20.7% | 18.5% | 14% | 32% | — | 17% | 22% |
| Modulus (psi) | 1.4×10^8 | 1.1×10^8 | 1.1×10^8 | 1.1×10^8 | 0.46×10^8 | — | — | 1.2×10^8 |
| Knot strength (psi) | 37,500 | 37,100 | 30,000 | 43,000 | 27,000 | — | 42,000 | 48,000 |
| Shrinkage (H ₂ O/77°C./5 min.) | 13% | 27.5—44% | 72% | 12% | 73% | — | ca. 15% | ca. 15% |
| Wt. loss (H ₂ O/100°C./50 hrs.) | 44% | 48% | 65% | 45% | — | — | — | — |

TABLE II (Continued)

| Examples | II | III | IV | V | VI | VII | VIII | IX |
|----------------------------|----------------------------------|--------|----|--------|----|-----|------|------|
| | After 30 days in water at 37°C.: | | | | | | | |
| Inh. visc. (drawn fil.) | — | 0.54 | — | 0.58 | — | — | 0.81 | 0.72 |
| Ten. strength (psi) | — | 23,800 | — | 26,000 | — | — | — | — |
| Wt. loss | — | 3.5% | — | 7.4% | — | — | 5.6% | 0.3% |
| | After 90 days in water at 37°C.: | | | | | | | |
| Inh. visc. (drawn fil.) | — | — | — | 0.34 | — | — | 0.58 | 0.35 |
| Ten. strength (psi) | — | — | — | 12,000 | — | — | — | — |
| Wt. loss | — | — | — | 12.1% | — | — | 7.1% | 3.5% |

EXAMPLES X—XI.

5 Copolymers of L-lactide with the intermolecular cyclic esters of α -hydroxybutyric acid and α -hydroxyheptanoic acid were made by essentially the method of Example I.

10 A mixture of 44.2 parts of L-lactide and 5.8 grams of the cyclic ester of α -hydroxybutyric acid was fused under nitrogen, and there was added 0.08 g. of 25% solution of diethylzinc in heptane. The mixture was heated at 105–108°C. for 3 hours at atmospheric pressure in an atmosphere of nitrogen. The resulting copolymer of L-lactide and the intermolecular cyclic ester of α -hydroxybutyric acid (88.4/11.6) had an inherent viscosity of 2.15 (0.1% solution in benzene).

20 The copolymer of L-lactide and the intermolecular cyclic ester of α -hydroxyheptanoic acid (90/10) was prepared similarly from 45 g. of L-lactide, 5 g. of cyclic ester, and 0.08 g. of 25% solution of diethylzinc in heptane. After the mixture was heated for 3 hours, the resulting polymer had an inherent viscosity of 2.28.

25 The spinning conditions and filament properties of these copolymers are summarized in Table III.

30 The intermolecular cyclic esters of α -hydroxybutyric acid and α -hydroxyheptanoic acid were prepared essentially by the method of Bischoff and Walden, Ann, 279, 100 (1895). The sodium salts of the corresponding α -

5 bromo acids were made from the acids and sodium methoxide in an ethyl ether/ethyl alcohol mixture. The cyclic esters were made by heating the sodium salts to 300—315°C. under reduced pressure. The butyric acid derivative was purified by distillation at 78—85°C./0.07 mm. and by crystallization from ethyl alcohol/petroleum ether, with cooling in solid carbon dioxide. The heptanoic acid derivative was purified by crystallization from pentane, with cooling in solid carbon dioxide, and from ethyl alcohol. Both cyclic esters were characterized by elemental analyses and infrared absorption spectra. 10

TABLE III

| Example | X | XI |
|---|--|--|
| % Comonomer | 11.6% Intermolecular cyclic ester of α -hydroxybutyric acid | 10% Intermolecular cyclic ester of α -hydroxyheptanoic acid |
| Inh. viscosity (bulk) | 2.15 | 2.28 |
| Spinning temperature | 185°C. | 190°C. |
| Draw ratio | 10* | 8 |
| Drawing temperature | 94°C., 122°C.* | 98°C. |
| Inherent viscosity | 1.42** | 1.63** |
| Tensile strength (psi) | 66,300 | 59,100 |
| Elongation at break | 22.3% | 18.3% |
| Modulus (psi) | 1.04×10^6 | 0.95×10^6 |
| Shrinkage (H ₂ O/77°C./5 min.) | 20.6% | 55.0% |
| Weight loss (H ₂ O/100°C./48 hrs.) | 60.5% | 63.6% |

* This filament was drawn in two stages. In the first stage it was drawn 7X (draw ratio of 7) at 94° C.; in the second, it was drawn at 122° C. to an extent sufficient to give an overall draw ratio of 10.

** Measured on undrawn filament. The inherent viscosities of the filaments of Examples V—XIII were measured on drawn filaments.

EXAMPLE XII.

20 A mixture of 206 g. of powdered L-lactide/DL-lactide (90/10) copolymer and 0.618 g. of the monosodium salt of 4-[4-(ethyl-*p*-sulphobenzylamino)diphenylmethylene][1 - (N-ethyl-N-*p*-sulphoniumbenzyl)- $\Delta^{2,5}$ - cyclohexadienimine][F D & C (food, Drug, and Cosmetic) Green No. 1] was rotated in a Fisher-Kendall mixer for 48 hours at room temperature. The resulting homogeneous mixture was pressed to a plug and spun into green monofilaments by essentially the method of Example I. The filaments were not annealed.

25 Sterilisation of the products of the Examples may be effected in any convenient way. In one such method the drawn, annealed filament is cut to convenient length, placed in polyethylene bags, which are sealed and exposed to two

passess under a Van de Graaff beam of 2 million electron volts. The bags may contain dry filament, or filament in water or filament in ethyl alcohol. 35

Although in the Examples bulk polymerization has been used in preparing the polylactides, it is to be understood that the polymerization can also be effected in solution or suspension. When the solution method is used, the ratio of monomer to solvent can be from 1:1 to 5:1. Suitable media are aromatic hydrocarbons such as the xylenes, and ethers such as tetrahydrofuran, dioxane, and 1,2-dimethoxyethane. 40 45

Although this invention has been more specifically illustrated with monofilaments, it is to be understood that the copolymer can be in the form of multifilaments, e.g., braided 50

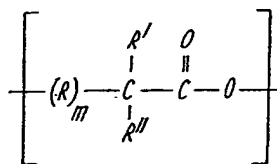
structures. The term "braided structure" is used to connote a structure formed by combining together two or more strands, i.e. filaments or ribbons. The strands can be braided to form useful sutures in any of a wide variety of ways such as, for example, in the manner customarily employed for making Manila rope, lanyards and the like. In the final braided suture, at least 50% of the individual strands should be oriented. Preferably 90% or more of the strands making up the braided structure should be oriented.

The products of the invention are useful in surgical applications where an absorbable aid or support is required, for example, in the formation of surgical mesh, absorbable staple, artificial tendons, or cartilage material, and in other uses where a temporary aid during healing is needed. They may also be used to advantage in repairing hernias and in anchoring organs which have become loose.

In the specification of our Patent No. 1,048,088 sutures formed from a sterile oriented synthetic polylactide having an inherent viscosity of at least 1.0 at 0.1% concentration by weight in benzene at 25°C, and being such that they shrink in length less than 15% when immersed in water at 77°C for five minutes, are described and claimed.

WHAT WE CLAIM IS:—

1. An oriented filament or ribbon suitable for use as or in a surgical suture, said filament or ribbon being composed of a lactide copolymer containing 85 to 98.5% of repeating units of a single antipodal species of alpha hydroxy propionic acid and 1.5 to 15% of repeating units of the formula:



where R is lower alkylene, m is 0 or 1, R' is a hydrogen atom or a lower alkyl group, and R'', which can be the same as or different from R', is a hydrogen atom or an alkyl group of up to 22 carbons when m is zero and, when m is 1, R'' is a hydrogen atom or a lower alkyl group, lower, herein meaning having up to 6 carbon atoms, and the repeating units of the said formula including at least one which is different from that derived from the said antipodal species, said copolymer before being oriented having an inherent viscosity of at least 1.0 at 0.1% concentration in benzene at 25°C. and said filament losing at least 20%

of its weight on treatment with boiling water for a period of 100 hours.

2. An oriented filament as claimed in claim 1, which has been formed by melt-extrusion and oriented by drawing, said filament having a tensile strength of 25,000 to 100,000 p.s.i.

3. A filament as claimed in claim 2 which has been annealed and shows less than 15% shrinkage when immersed without tension in water at 77°C.

4. A filament as claimed in claim 2 or 3, wherein the copolymer contains up to 12% of repeating units derived from glycolide.

5. A filament as claimed in claim 2 or 3 wherein the copolymer is a poly-L(-)-lactide copolymer containing up to 15% of repeating units derived from DL-lactide.

6. A filament as claimed in claim 2 or 3 wherein the copolymer is a 95/5 copolymer of L(-)-lactide and DL-lactide.

7. A filament as claimed in any preceding claim containing a minor proportion of an inert colouring agent and plasticizer.

8. A filament as claimed in claim 7 containing glyceryl triacetate as a plasticizer.

9. A surgical suture composed of a monofilament as claimed in any preceding claim, having a diameter of 0.1 to 45 mils and a tensile strength of 25,000 to 100,000 p.s.i.

10. A suture as claimed in claim 9 having a diameter of 1—20 mils.

11. A surgical suture comprising a plurality of filaments as claimed in any one of claims 1 to 8 braided together.

12. A surgical suture as claimed in claim 11, including also a plurality of unoriented filaments of said copolymer, the oriented filaments comprising in number at least 50% of the braided suture.

13. A surgical suture as claimed in claim 10 or 11, in which the individual filaments have diameters in the range 0.1 to 45 mils and which has a tensile strength of 25,000 to 100,000 p.s.i.

14. Filaments according to claim 1, and surgical sutures containing such filaments, substantially as hereinbefore described.

15. A process for making oriented filaments as claimed in any one of claims 2 to 6 comprising melt-extruding the copolymer through a spinneret and effecting orientation of resulting filaments by drawing them at 70 to 140°C to at least 5 times and not more than 11 times their original length.

16. A process according to claim 15, wherein the oriented filament is annealed to 60 to 150°C while held substantially taut until it shows less than 15% shrinkage on subsequent immersion without tension in water at 77°C.

17. A process for preparing a filament claimed in claim 1, substantially as hereinbefore described.

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